

### In the Claims.

The following list of Claims replaces all prior versions.

What is claimed is:

- 1) (original) A method of determining the pH of a sample, comprising:
  - a) Determining an infrared spectrum of the sample;
  - b) Determining the concentration of hemoglobin of the sample;
  - c) Selecting a model relating an infrared spectrum to pH that is applicable for samples having the determined hemoglobin concentration;
  - d) Determining the pH of the sample from the infrared spectrum and the selected model.
- 2) (original) A method as in Claim 1, wherein the model comprises regression coefficients relating an infrared spectrum to sample pH.
- 3) (original) A method as in Claim 1, wherein the model comprises a model determined from calibration data collected from samples with hemoglobin levels spanning the range of sample hemoglobin levels.
- 4) (original) A method as in Claim 1, wherein the model comprises a model determined from hemoglobin-specific regression coefficients applied to calibration data collected from samples with hemoglobin levels that do not span the sample hemoglobin range.
- 5) (original) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transmittance, ATR.
- 6) (cancelled)
- 7) (currently amended) A method as in Claim 1, A method of determining the pH of a sample, comprising:
  - a) Determining an infrared spectrum of the sample;
  - b) Determining the concentration of hemoglobin of the sample;
  - c) Selecting a model relating an infrared spectrum to pH that is applicable for samples having the determined hemoglobin concentration;
  - d) Determining the pH of the sample from the infrared spectrum and the selected model;

wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 25000-11000 cm<sup>-1</sup>.
- 8) (currently amended) A method as in Claim 47, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 8000 cm<sup>-1</sup>.
- 9) (currently amended) A method as in Claim 48, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 6000 – 6500 cm<sup>-1</sup>.
- 10) (original) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation at a spectral resolution of 64 cm<sup>-1</sup> or finer.
- 11) (currently amended) A method as in Claim 1, wherein determining the concentration of hemoglobin comprises at least one of:
  - a) Direct measurement of a blood sample using an external instrument or method;
  - b) Spectroscopic measurement of a blood sample; and
  - ~~c) Noninvasive measurement of perfused tissue.~~
- 12) (original) A method as in Claim 1, wherein determining the concentration of hemoglobin comprises at least one of:
  - a) Measuring the sample hemoglobin concentration under physiological conditions that are not undergoing rapid change;

- b) Accounting for errors introduced by potentially interfering intravascular substances.
- 13) (original) A method as in Claim 1, wherein the sample comprises at least one of:
- a) A blood sample drawn from the patient;
  - b) A blood sample measured intravascularly (indwelling measurement);
  - c) Perfused tissue;
  - d) Perfused skin;
  - e) An ex vivo blood sample in a transmission vessel;
  - f) An ex vivo blood sample in a transfectance vessel;
  - g) A blood sample in an on-line flow circuit;
  - h) In situ measurement of a perfused tissue; and
  - i) In situ measurement of a perfused organ or muscle.
- 14) (currently amended) A method of determining pH of a sample, comprising:
- a) Determining an infrared spectrum of the sample;
  - b) Verifying that the spectrum is spectrally consistent with the calibration model;
  - c) Determining the concentration of hemoglobin, hematocrit, or equivalent of the sample;
  - d) Determining the pH of the sample from the infrared spectrum, the determined hemoglobin, hematocrit, or equivalent concentration, and a model relating an infrared spectrum and associated hemoglobin concentration to pH.
- 15) (original) A method as in Claim 14, wherein the model comprises regression coefficients relating an infrared spectrum to sample pH.
- 16) (original) A method as in Claim 14, wherein the model comprises a model determined from calibration data collected from samples with hemoglobin levels spanning the range of sample hemoglobin levels.
- 17) (original) A method as in Claim 14, wherein the model comprises a model determined from hemoglobin-specific regression coefficients applied to calibration data collected from samples with hemoglobin levels that do not span the sample hemoglobin range.
- 18) (original) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transfectance, ATR.
- 19) (original) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transfectance, ATR.
- 20) (currently amended) ~~A method as in Claim 14,~~ A method of determining pH of a sample, comprising:
- a) Determining an infrared spectrum of the sample;
  - b) Verifying that the spectrum is spectrally consistent with the calibration model;
  - c) Determining the concentration of hemoglobin, hematocrit, or equivalent of the sample;
  - d) Determining the pH of the sample from the infrared spectrum, the determined hemoglobin, hematocrit, or equivalent concentration, and a model relating an infrared spectrum and associated hemoglobin concentration to pH;
- wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 25000 11000 cm<sup>-1</sup>.
- 21) (currently amended) A method as in Claim ~~14~~20, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 8000 cm<sup>-1</sup>.

22) (currently amended) A method as in Claim 14~~21~~, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 6000 – 6500 cm<sup>-1</sup>.

23) (original) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation at a spectral resolution of 64 cm<sup>-1</sup> or finer.

24) (currently amended) A method as in Claim 14, wherein determining the concentration of hemoglobin comprises at least one of:

- a) Direct measurement of a blood sample using an external instrument or method;
- b) Spectroscopic measurement of a blood sample; and
- c) ~~Noninvasive measurement of perfused tissue.~~

25) (original) A method as in Claim 14, wherein determining the concentration of hemoglobin comprises at least one of:

- a) Measuring the sample hemoglobin concentration under physiological conditions that are not undergoing rapid change;
- b) Accounting for errors introduced by potentially interfering intravascular substances.

26) (original) A method as in Claim 14, wherein the sample comprises at least one of:

- a) A blood sample drawn from the patient;
- b) A blood sample measured intravascularly (indwelling measurement);
- c) Perfused tissue;
- d) Perfused skin;
- e) An ex vivo blood sample in a transmission vessel;
- f) An ex vivo blood sample in a transfectance vessel;
- g) A blood sample in an on-line flow circuit;
- h) In situ measurement of a perfused tissue; and
- i) In situ measurement of a perfused organ or muscle.

27) (cancelled)

28) (currently amended) ~~An apparatus as in Claim 27;~~ An apparatus for determining the pH of a sample, comprising:

- a) An illumination system adapted to direct radiation to the sample;
- b) A collection system adapted to receive radiation expressed from the sample responsive to incident radiation;
- c) An analysis system, comprising a model relating two or more of radiation expressed, incident radiation, and hemoglobin concentration to sample pH;

wherein:

- a<sub>d</sub>) The infrared radiation encompasses the spectral frequency range between 4000 – 25000 cm<sup>-1</sup>;
- b<sub>e</sub>) Infrared radiation is delivered to the sample through at least one of: optical fibers, light guides, and imaging optics;
- c<sub>f</sub>) Hemoglobin concentration is determined using radiation in the spectral frequency range from 10,000 – 25,000 cm<sup>-1</sup>; and
- c<sub>g</sub>) pH is determined using radiation in the spectral frequency range from 4,000 – 10,000 cm<sup>-1</sup> combined with the hemoglobin concentration.

29) (cancelled)